



1652

Attorney's Docket No.: 06497-013002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : James C. Liao
Serial No. : 10/048,186
Filed : June 19, 2002
Title : ENGINEERING OF METABOLIC CONTROL

Art Unit : 1652
Examiner : Unknown

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Commissioner for Patents
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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Applicant discloses the references listed on the attached form PTO-1449. Enclosed is a copy of a search report dated June 6, 2003, issued in a counterpart international application EP 00950804.5.

This statement is being filed before the receipt of a first Office action on the merits.
Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 7-18-03

Y. Rocky Tsao
Y. Rocky Tsao
Reg. No. 34,053

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

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CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Sheet 1 of 1

| | | | |
|--|--|---------------------------------------|-------------------------------|
| Substitute Form PTO-1449 (Modified) | | Attorney's Docket No. 06497-013002 | Application No. 10/048,186 |
| Information Disclosure Statement by Applicant (Use several sheets if necessary) (37 CFR §1.98(b)) | | Applicant James C. Liao | |
| | | Filing Date June 19, 2002 | Group Art Unit 1652 |

| U.S. Patent Documents | | | | | | | |
|------------------------------|-----------|-----------------|------------------|----------|-------|----------|----------------------------|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee | Class | Subclass | Filing Date If Appropriate |
| | CA | | | | | | |
| | CB | | | | | | |
| | CC | | | | | | |
| | CD | | | | | | |
| | CE | | | | | | |
| | CF | | | | | | |
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| Foreign Patent Documents or Published Foreign Patent Applications | | | | | | | |
|--|-----------|-----------------|------------------|--------------------------|-------|----------|----------------------------|
| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation Yes No |
| | CL | | | | | | |
| | CM | | | | | | |
| | CN | | | | | | |
| | CO | | | | | | |
| | CP | | | | | | |

| Other Documents (include Author, Title, Date, and Place of Publication) | | |
|--|-----------|---|
| Examiner Initial | Desig. ID | Document |
| | CQ | Reitzer et al., "Expression of <i>glnA</i> in <i>Escherichia coli</i> is regulated at tandem promoters", <i>Proc. Natl. Acad. Sci. USA</i> 82:1979-1983 (1985) |
| | CR | Wanner et al., "Involvement of Phosphotransacetylase, Acetate Kinase, and Acetyl Phosphate Synthesis in Control of the Phosphate Regulon in <i>Escherichia coli</i> ", <i>J. Bacteriol.</i> 174(7):2124-2130 (1992) |
| | CS | |
| | CT | |

| | |
|--|-----------------|
| Examiner Signature | Date Considered |
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | |

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NR. 064

P03



P.B. 5018 - Patentanwalt
2280 HV Rijswijk (ZH)
T: (070) 340 2040
Tx 51651 epo nl
FAX (070) 340 3018

ANWÄLTE

EING.: 10. Juni 2003

Teilname:

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GROSSE BOCKHORNI SCHUMACHER
Patent- und Rechtsanwälte
Forstenrieder Allee 59
81476 München
ALLEMAGNE

Datum/Date

06.06.03

| | |
|---|---|
| Zeichen/Ref./Réf. E 78229 EP (GS) | Anmeldung Nr./Application No./Demande n°//Patent Nr./Patent No./Brevet n° 00950804.5-2401/US0020519 |
| Ansökande/Applicant/Demandeur//Patentinhaber/Propriétaire/Titulaire EDOCA Industry Research and Development Institute | |

COMMUNICATION

The European Patent Office herewith transmits the supplementary partial European search report under Rule 46(1) EPC relating to the above mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869,-) or the equivalent applicable on the date of payment is payable.
This applies also to the search fees requested under Rule 46(1) EPC:
See also OJ EPO 06/1999, 405.

The abstract was modified by the Search Division and the definitive text is attached to the present communication.

Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

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| E 2 | |
| E 3 | 25.06.03 |
| Frist: 10.07.03 | |

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245. Redaktionsschluß

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Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER



European Patent
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**SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT**
under Rule 46, paragraph 1 of the European Patent Convention

Application Number

EP 00 95 0804

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | |
|--|---|--|--|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int.Cl.) |
| Y | <p>REITZER L J ET AL: "EXPRESSION OF GLN-A IN ESCHERICHIA-COLI IS REGULATED AT TANDEM PROMOTERS". PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 82, no. 7, 1985, pages 1979-1983, XP009007332 1985 ISSN: 0027-8424 abstract, p. 1979-1980, 1982</p> | 1-8, 17-20, 24, 30-34 | C12N1/21 C12N15/52 C12P23/00 C12P5/02 C12Q1/68 |
| Y,D | <p>FENG JUNLI ET AL: "Role of phosphorylation metabolic intermediates in the regulation of glutamine synthetase synthesis in Escherichia coli." JOURNAL OF BACTERIOLOGY, vol. 174, no. 19, 1992, pages 6061-6070, XP009007255 ISSN: 0021-9193 abstract, p. 6061-6062, 6064-6065, 6067</p> | 1-8, 17-20, 24, 30-34 -/- | TECHNICAL FIELDS SEARCHED (Int.Cl.) |
| | | | C12N C12P |
| LACK OF UNITY OF INVENTION | | | |
| <p>The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:</p> <p>see sheet B</p> | | | |
| <p>The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.</p> | | | |
| 1 | Place of search MUNICH | Date of completion of the search 27 May 2003 | Examiner Puonti-Kaerlas, J |
| <p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p> | | | |



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**SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT**

Application Number
EP 00 95 0804

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | CLASSIFICATION OF THE APPLICATION (Int.Cl.) |
|--|--|--------------------------|--|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | TECHNICAL FIELDS SEARCHED (Int.Cl.) |
| A | <p>WANNER B L ET AL: "INVOLVEMENT OF PHOSPHOTRANSACETYLASE ACETATE KINASE AND ACETYL PHOSPHATE SYNTHESIS IN CONTROL OF THE PHOSPHATE REGULON IN ESCHERICHIA-COLI" JOURNAL OF BACTERIOLOGY, vol. 174, no. 7, 1992, pages 2124-2130, XP009007331 ISSN: 0021-9193</p> | | |



European Patent
Office

LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 00 95 0804

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-8, 24 (complete), 17-20, 30-34 (partially)

A bacterial host cell comprising a nucleic acid comprising a promoter which is controlled by a response regulator protein, the host being genetically modified such that said promoter is regulated by acetyl phosphate in the absence of nitrogen starvation, and subject-matter related thereto.

**2. Claims: 9, 14-16, 21 (complete), 10-13, 17-20, 27-29,
35 (partially)**

A host cell comprising a first expression cassette comprising a promoter which is controlled by acetyl phosphate in the absence of nitrogen starvation and a nucleic acid sequence encoding a first enzyme required for biosynthesis of a heterologous metabolite, as well as nucleic acid sequences encoding other enzymes required for the synthesis of said metabolite, and subject-matter related thereto.

3. Claim : 22 (complete)

A method of producing heterologous isoprenoids in a host cell by overexpressing phosphoenolpyruvate synthase and biosynthetic enzymes required for the synthesis of the isoprenoids.

4. Claim : 23 (complete)

A method of producing lycopene in a host cell by expressing a heterologous 1-deoxy-D-xylulose 5-phosphate synthase, geranylgeranyl diphosphate synthase, phytoene synthase and phytoene desaturase.

5. Claims: 25-26 (complete), 27-35 (partially)

A nucleic acid sequence comprising a promoter and a sequence encoding an enzyme required for the production of a first metabolite, said promoter being regulated by a second metabolite, the concentration of which is indicative of availability of a precursor for the synthesis of the first metabolite, and subject-matter related thereto.